**Minutes of IARC meeting 97, April 11th, 2022**

In attendance: Ayelet Peres, Gur Yaari, Martin Corcoran, William Lees, Mats Ohlin, James Heather (guest)

1. **Approval of minutes of meeting 95**
   Approved

2. **Approval of minutes of meeting 96**
   Approved

3. **Draft report to AIRR-C Meeting VI**
   Discussion of the report and its content

4. **Assessment of inference in S00036 - sequences not to be considered at this stage**

   Few sequences supported three inferences of submission S00036 and they will not be considered further as they are not likely to reach affirmation level 0:
   TRBV12-1*01_C165A in P4_I11_S1 - 3 sequences
   TRBV12-2*01_T187C in P4_I16_S1 - 7 sequences
   TRBV6-9*01_A303G in P4_I31_S1 - 8 sequences

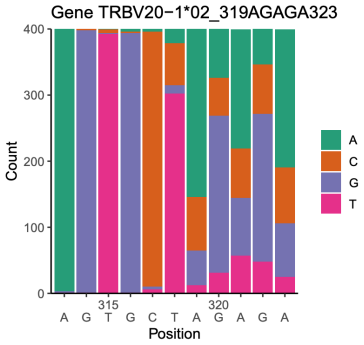
   These inferences were extensions only but might be considered later
   TRBV20-1*02_319AGAGA323 in P4_I1_S1
   TRBV2*02_322GAAGC326 in P4_I1_S1

5. **Consideration of example the 3'-end of alleles of TRBV (extracted from OGRDBStats plots on April 7th, 2022)**

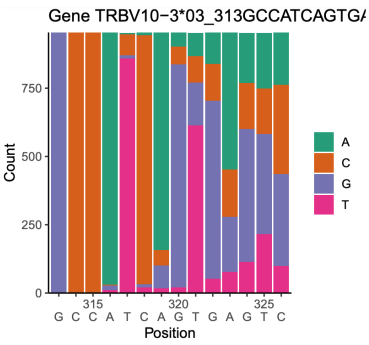
   Substantial variability in the ability to infer 3'-nucleotides exists. Commonly several bases cannot be inferred as consistently as 3' bases of alleles of IGHV genes. Occasionally unexpected outcomes, as in TRBV12-4*01_C87T in P4_I30_S1, are linked to a fact that the underlying data is not appropriate (dominance of certain rearrangements and/or presence of many reads not perfectly matching the allele in question). Discussion on the importance of upholding affirmation only of bases for which there is solid evidence while databases may carry the full length sequences as there typically is limited

diversity among alleles at the 3’-end. AP will assess the possibility to even more stringently remove multiple occurrences of highly expanded clones during the analysis step to better grasp the nature of the 3’-end.

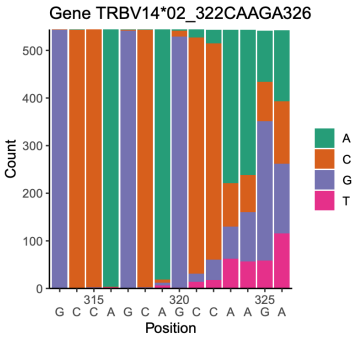
P4_I10_S1



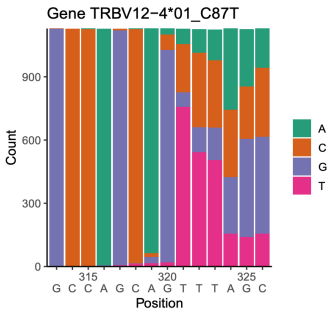

P4_I11_S1



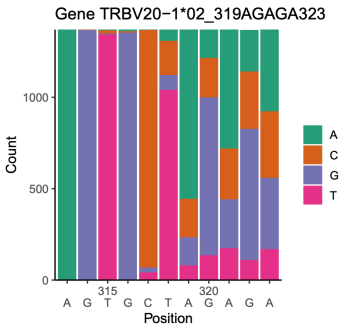

P4_I11_S1



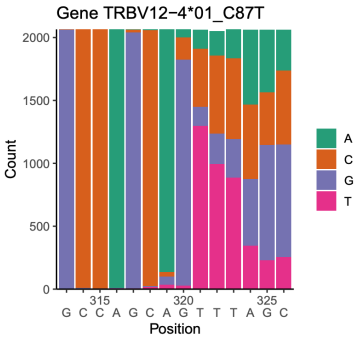

P4_I11_S1



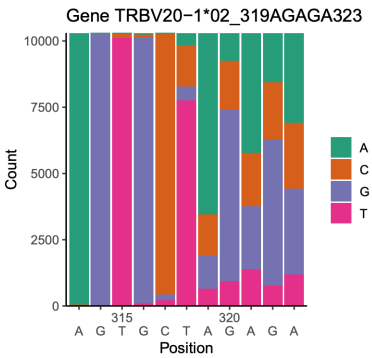

P4_I12_S1



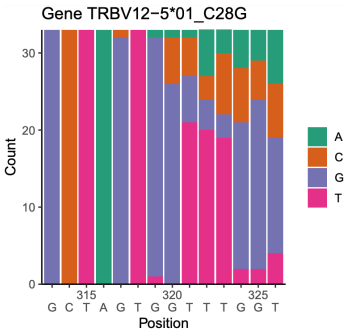

P4_I13_S1



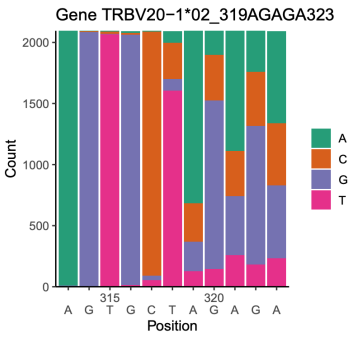

P4_I13_S1



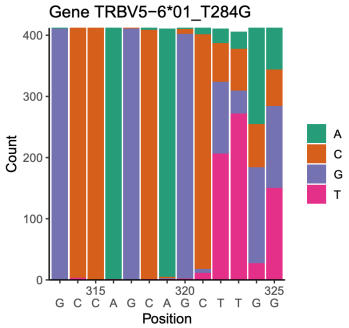

P4_I17_S1



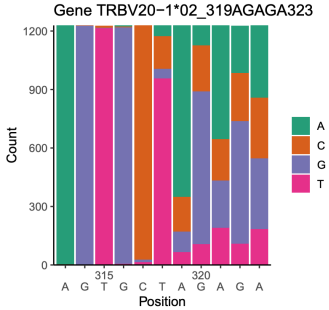

P4_I17_S1



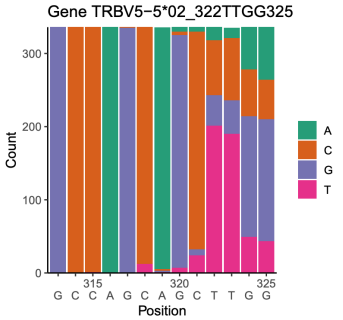

P4_I17_S1



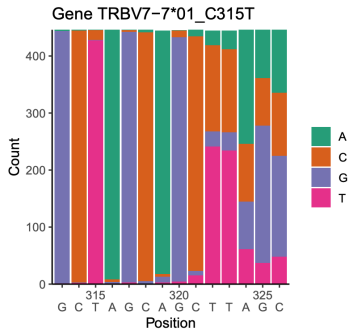

P4_I18_S1



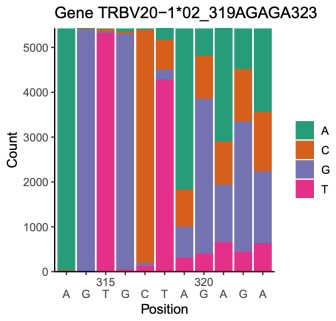

P4_I18_S1



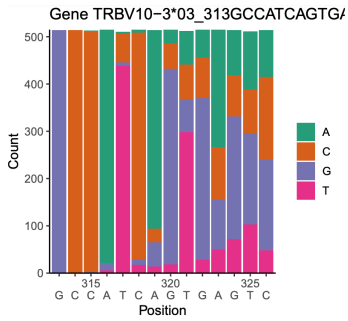
P4_I19_S1



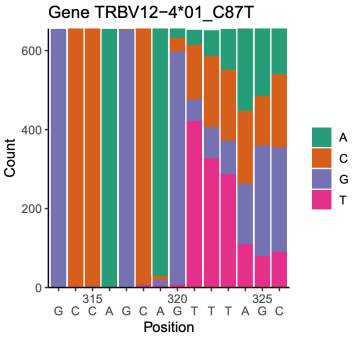

P4_I1_S1



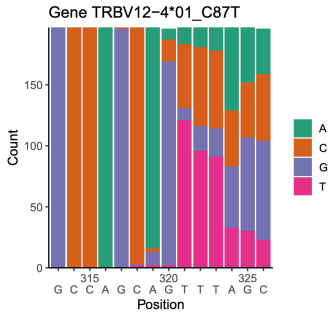

P4_I24_S1



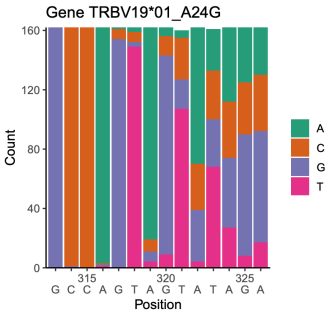

P4_I24_S1



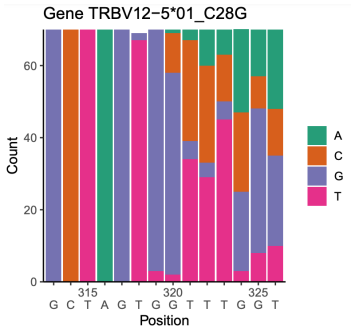

P4_I25_S1



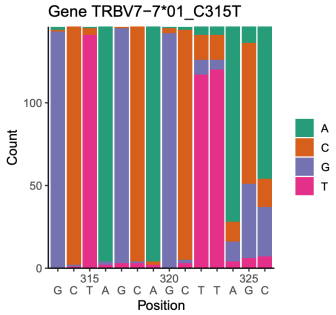

P4_I25_S1



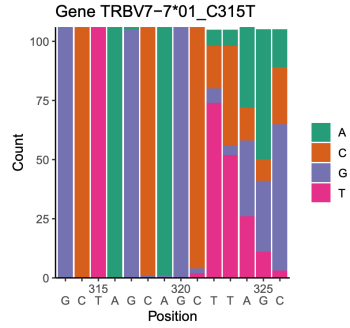

P4_I27_S1



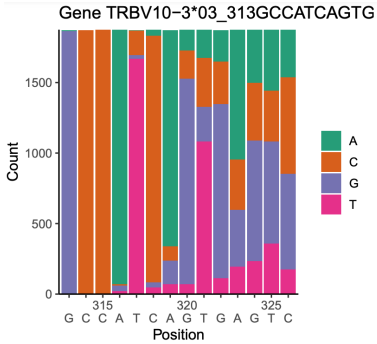

P4_I27_S1



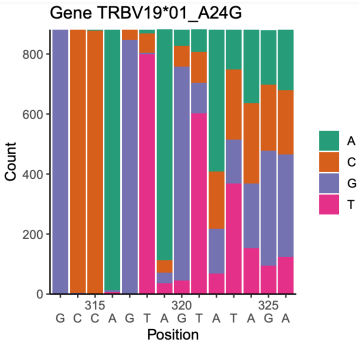

P4_I29_S1




P4_I2_S1

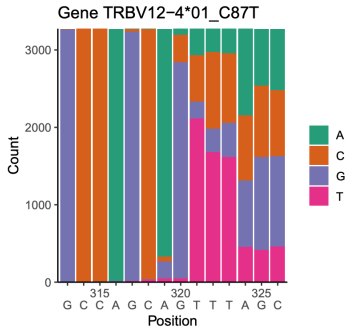


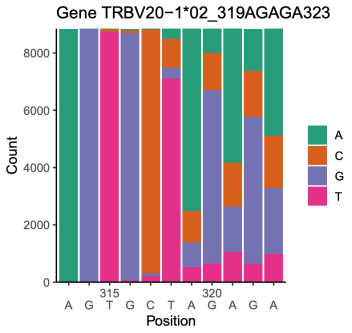

P4_I2_S1



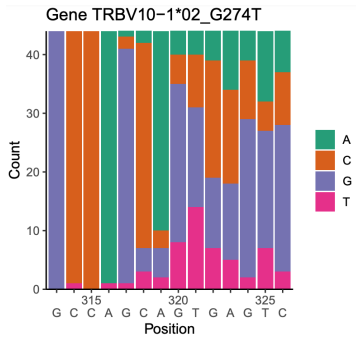

P4_I2_S1

P4_I2_S1

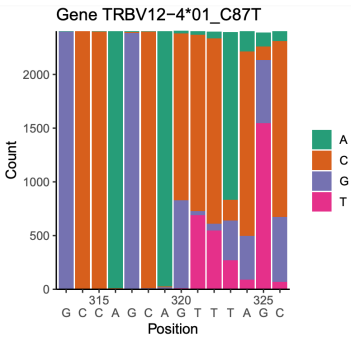


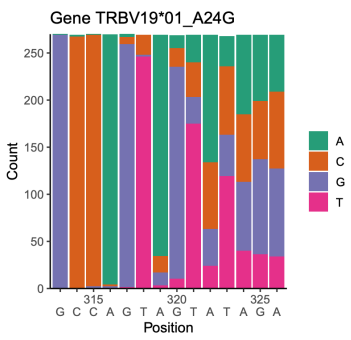

P4_I30_S1

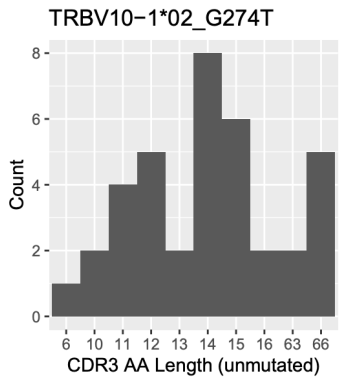


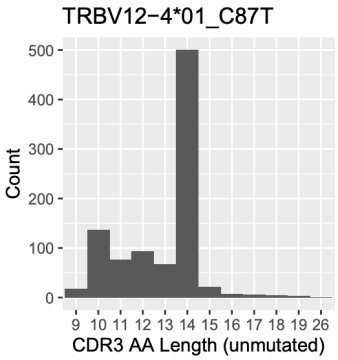

P4_I30_S1

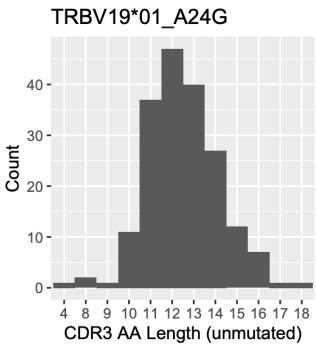



P4_I30_S1



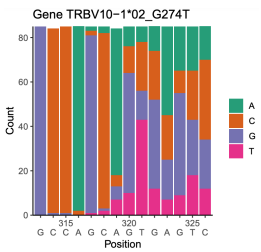



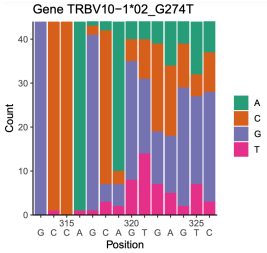
Examples of similarity of perceived 3’-ends between different sets of data:

## TRBV10-1*02_G274T

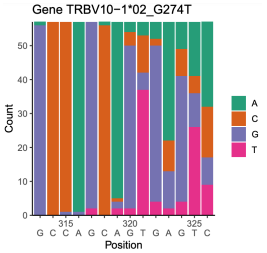
P4_I15_S1



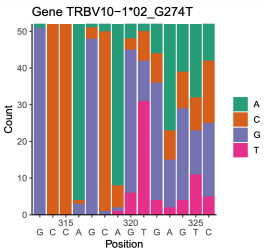

P4_I30_S1




P4_I31_S1



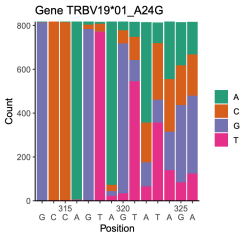

P16_I1_S1



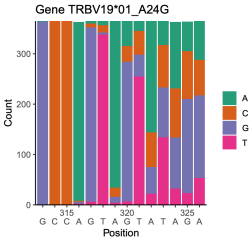

---

## TRBV19*01_A24G

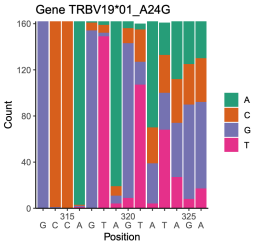
P4_I11_S1



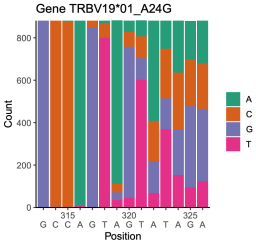

P4_I24_S1



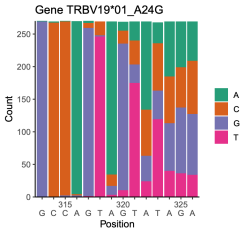

P4_I25_S1



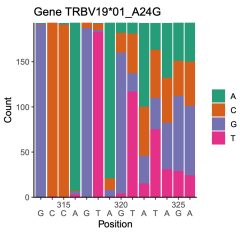

P4_I2_S1



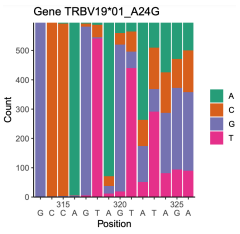

P4_I30-S1




P4_I31_S1



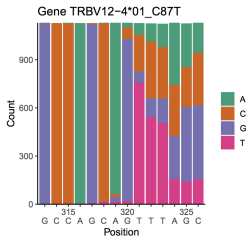

P16-I3_S1



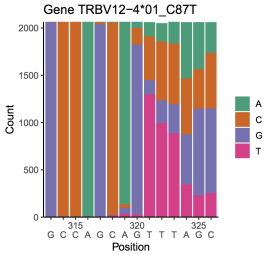

---

## TRBV12-4*01_C87T

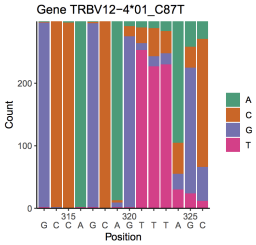
P4_I11_S1



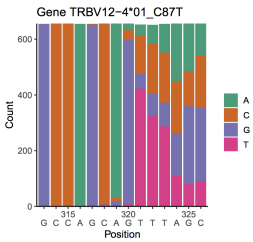

P4_I13_S1



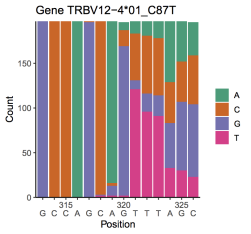

P4_I22_S1



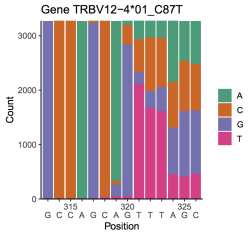

P4_I24_S1



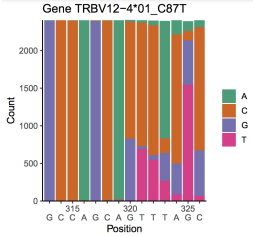

P4_I25_S1



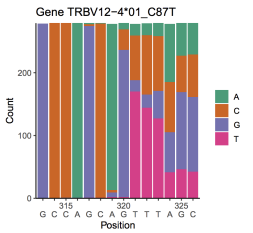

P4_I2_S1



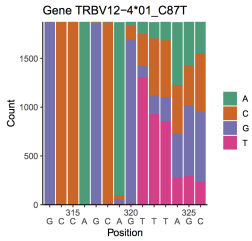

P4_I30_S1



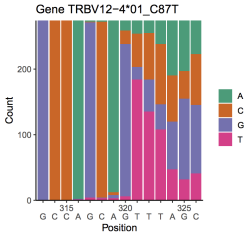

P4_I31_S1



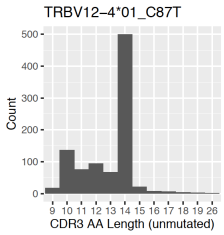

P4_I4_S1



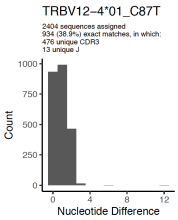

P16_I3_S1



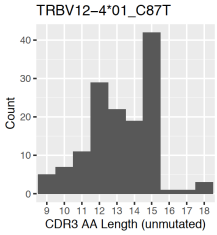

P4_I30_S1



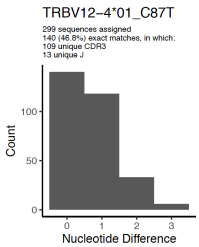

P4_I30_S1



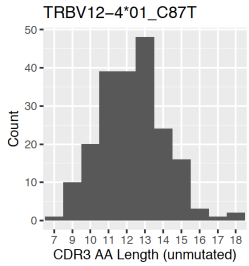

P4_I22_S1



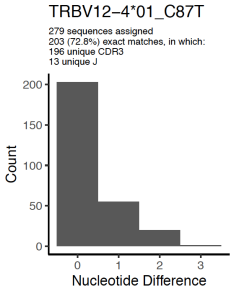

P4_I22_S1



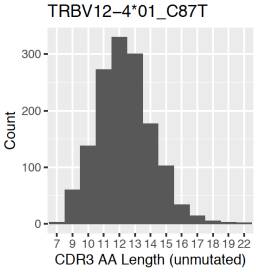

P4_I31_S1



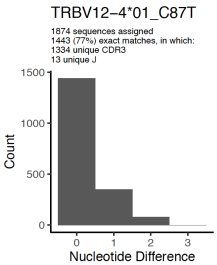

P4_I31_S1




P4_I4_S1




P4_I4_S1




(Note: the data for P4_I22_S1, P4_I30_S1 seem to be of low quality with many sequences scored with one or more difference from the inferred allele)

## 6. Assessment of inference TRBV19*01_A24G in P4_I24_S1 (S00036)

Provisional assessment, to be re-considered at Meeting 98: TRBV19*01_A24G has been inferred in six genotypes in the VDJbase P4 data set, including in VDJbase P4_I24_S1, a haplotypable data set (based on heterozygocity in TRBJ1-6). The genotype is also implied to carry TRBV19*01. No other gene in the IMGT database is closely related to these alleles of TRBV19. The novel allele is the most expressed allele in the repertoire (53% allelic frequency; 0.71% of the total error-free population). It is represented by 240 error-free sequences and 202 unique CDR3s in the error-free set. Haplotyping based on allelic diversity in TRBJ1-6 demonstrates perfect separation from TRBV19*01. IARC provisionally affirms the sequence up to and including base 322. It is acknowledged that the allele most likely carries 4 additional bases, typically TAGA, at base positions 323-326. Trailing "." indicates IARC's opinion that the sequence is likely to contain additional 3'-nucleotides for which there is insufficient evidence to make an affirmation.

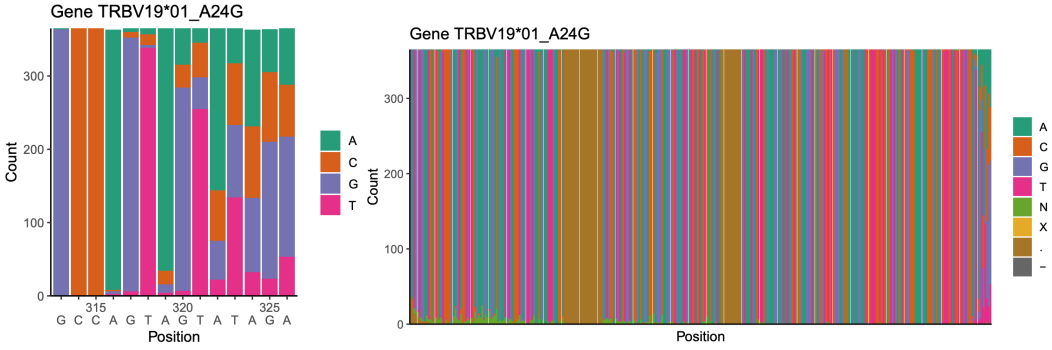
```
>TRBV19*01_A24G
GATGGTGGAATCACTCAGTCCCCGAAGTACCTGTTCAGAAAGGAAGGACAGAATGTG
ACCCTGAGTTGTGAACAGAATTTGAACCACGATGCCATGTACTGGTACCGACAGGAC
CCAGGGCAAGGGCTGAGATTGATCTACTACTCACAGATAGTAAATGACTTTCAGAAA
GGAGATATAGCTGAAGGGTACAGCGTCTCTCGGGAGAAGAAGGAATCCTTTCCTCTC
ACTGTGACATCGGCCCAAAAGAACCCGACAGCTTTCTATCTCTGTGCCAGTAGTA..
..
```

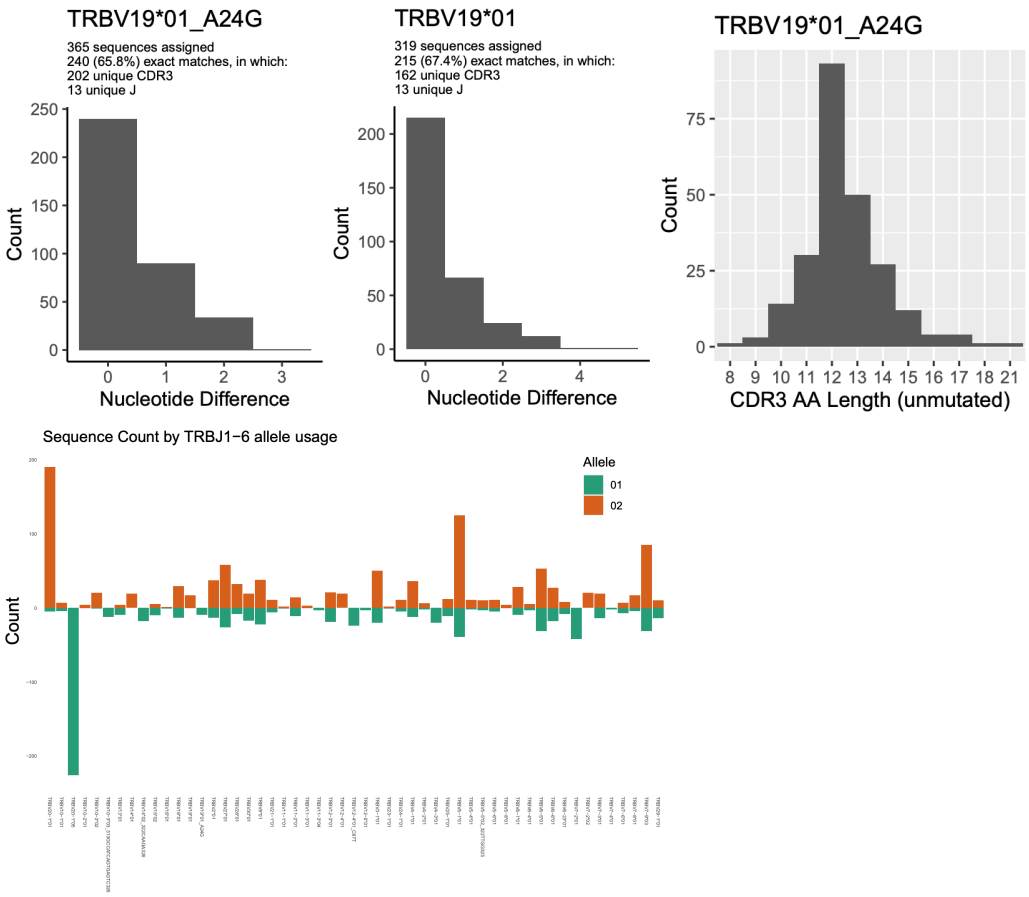
| Result summary: TRBV19*01_A24G | No rearrangement found | | |
|---|---|---|---|
| V-GENE and allele | Homsap TRBV19*01 F | score = 1356 | identity = 99.63% (272/273 nt) |
| FR-IMGT lengths, CDR-IMGT lengths | [5.6.X] | | |

### 1. Alignment for V-GENE and allele identification

**Closest V-REGIONs** (evaluated from the V-REGION first nucleotide to the 2nd-CYS codon)

| | | Score | Identity |
|---|---|---|---|
| L36092 | Homsap TRBV19*01 F | 1356 | 99.63% (272/273 nt) |
| M97725 | Homsap TRBV19*03 (F) | 1347 | 99.27% (271/273 nt) |
| U48259 | Homsap TRBV19*02 F | 1338 | 98.90% (270/273 nt) |
| L33102 | Homsap TRBV10-3*04 [F] | 510 | 65.20% (178/273 nt) |
| U08314 | Homsap TRBV28*01 F | 510 | 65.20% (178/273 nt) |






7. **Assessment of inference TRBV12-4*01_C87T in P4_I24_S1 (S00036)**
   Provisional assessment, to be re-considered at Meeting 98: TRBV12-4*01_C87T has been inferred in nine genotypes in the VDJbase P4 data set, including in VDJbase P4_I24_S1, a haplotypable data set (based on heterozygocity in TRBJ1-6). The genotype is also implied to carry TRBV12-4*01. No other gene apart from TRBV12-3 in the IMGT database is closely related to these alleles of TRBV12-4. The novel allele is the most expressed allele in the repertoire (72% allelic frequency; 1.47% of the total error-free population). It is represented by 499 error-free sequences and 467 unique CDR3s in the error-free set. Haplotyping based on allelic diversity in TRBJ1-6 demonstrates perfect separation from TRBV12-4*01. IARC provisionally affirms the sequence up to and including base 321. It is acknowledged that the allele most likely carries 5 additional bases, typically TTAGC, at base positions 322-326. Trailing “.” indicates IARC’s opinion that the sequence is likely to contain additional 3’-nucleotides for which there is insufficient evidence to make an affirmation.

```
>TRBV12-4*01_C87T
GATGCTGGAGTTATCCAGTCACCCCGGCACGAGGTGACAGAGATGGGACAAGAAGTG
ACTCTGAGATGTAAACCAATTTCAGGACATGACTACCTTTTCTGGTACAGACAGACC
```

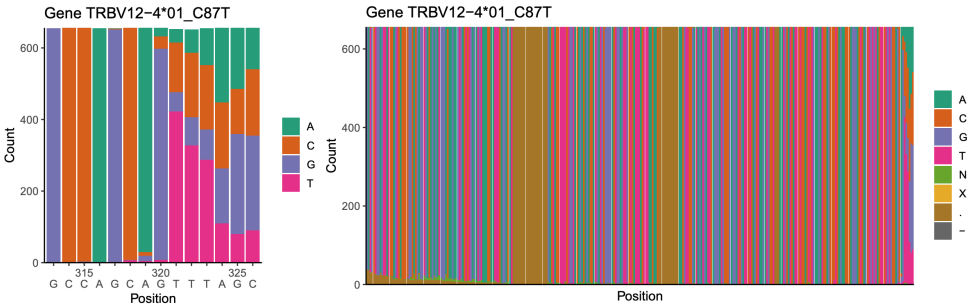
ATGATGCGGGGACTGGAGTTGCTCATTTACTTTAACAACAACGTTCCGATAGATGAT
TCAGGGATGCCCGAGGATCGATTCTCAGCTAAGATGCCTAATGCATCATTCTCCACT
CTGAAGATCCAGCCCTCAGAACCCAGGGACTCAGCTGTGTACTTCTGTGCCAGCAGT
. . . . .

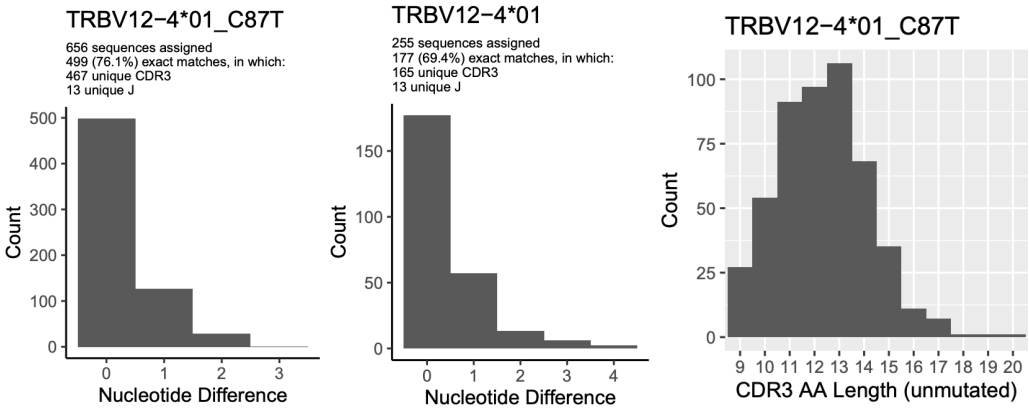
| **Result summary:** TRBV12-4*01_C87T | No rearrangement found | | |
|---|---|---|---|
| V-GENE and allele | Homsap TRBV12-4*01 F, or Homsap TRBV12-4*02 (F) | score = 1371 | identity = 99.64% (275/276 nt) |
| FR-IMGT lengths, CDR-IMGT lengths | [5.6.X] | | |

## 1. Alignment for V-GENE and allele identification

**Closest V-REGIONs** (evaluated from the V-REGION first nucleotide to the 2nd-CYS codon)

| | | Score | Identity |
|---|---|---|---|
| X02546 | Homsap TRBV12-4*01 F | 1371 | 99.64% (275/276 nt) |
| M14264 | Homsap TRBV12-4*02 (F) | 1371 | 99.64% (275/276 nt) |
| X07192 | Homsap TRBV12-3*01 F | 1326 | 97.83% (270/276 nt) |
| X07223 | Homsap TRBV12-5*01 F | 957 | 82.97% (229/276 nt) |
| X07224 | Homsap TRBV12-1*01 P | 867 | 79.35% (219/276 nt) |

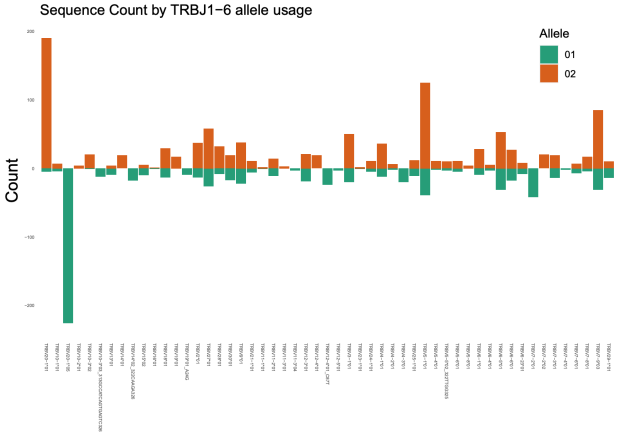








8. **Next meeting**
   April 19th, 2022 at 10.00 UTC